

Enzymatic Photocatalysis: Engineering Stereoselective Artificial Photoenzymes Based on Triplet Energy Transfer

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Light-induced transformations provide a powerful approach to deliver enantiopure building blocks in an atom-efficient manner. The Bach group has provided several examples of such enantioselective transformations using a chiral photosensitizer[1]. Their bifunctional catalyst combines a chiral substrate recognition motif with the versatile triplet sensitizer thioxanthone. Motivated by this achievement, our project aims to adapt this concept to the world of proteins, capitalizing on their inherent chirality to create an artificial photoenzyme.

We selected potential natural and *de novo* protein scaffolds based on their stability and previous reports on evolvability. After introducing cysteines at defined positions in the protein sequence, the photosensitizer is covalently linked to the protein by cysteine-maleimide or cysteine-haloacetamide bioconjugation chemistry (Fig. 1). Mass spectrometry verified successful protein labelling. Both [2+2]-photocycloadditions and deracemization reactions give promising initial results. For example, in [2+2]-photocycloadditions[2] and aza-Paternò-Büchi reactions[3], we achieved enantiomeric excesses of the formed products in the range of 10-40 % so far. In the future, we aim to improve these artificial photoenzymes via directed evolution.

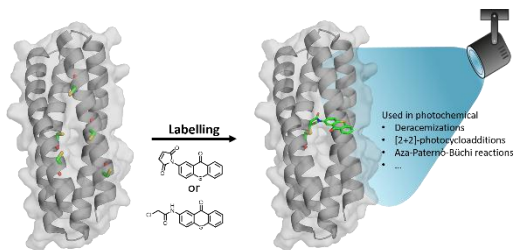


Figure 1: The photosensitizer, covalently bound to the protein via cysteine bioconjugation, promotes the light-induced triplet energy transfer (EnT) to a substrate. This enables both deracemizations as well as [2+2]-photocycloadditions.

[1] J. Großkopf *et al.*, Chem. Rev., 2021, **122**, 1626, 10.1021/acs.chemrev.1c00272.

[2] R. Alonso *et al.*, Angew. Chem. Int. Ed. 2014, **53**, 4368, 10.1002/anie.201310997.

[3] X. Li *et al.*, Angew. Chem. Int. Ed. 2021, **60**, 2684, 10.1002/anie.202013276.